

Results: High salt administration increased SAP compared with low salt in sham-operated (168 ± 4 mm Hg versus 149 ± 3 mm Hg, $P < 0.001$) or carotid-ligated rats (202 ± 5 mm Hg versus 153 ± 2 mm Hg, $P < 0.0001$). SAP, urinary excretion of vasopressin and norepinephrine, and expression of renin, angiotensin converting enzyme, and angiotensin II type-1 receptor messenger RNAs in the hypothalamus but not in the lower brainstem were greater in carotid-ligated than in sham-operated rats treated with high salt, whereas these parameters did not differ between the rats treated with low salt. Increases in SAP and urinary excretion of vasopressin and norepinephrine were completely inhibited by intracerebroventricular continuous infusion of CV-11974 in carotid-ligated rats administered with high-salt.

Conclusion: Chronic reduction of carotid blood flow may cause salt-sensitive hypertension via activation of the RAS in the hypothalamus of rats.

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Conduit Vessel Stiffness Is Increased in Central But Not Peripheral Conduit Arteries in Adults With Essential Hypertension

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Background: The status of conduit vessel stiffness in hypertension is controversial, possibly as a result of differential changes in central and peripheral conduit vessel properties.

Methods: Using calibrated tonometry and pulsed Doppler, we evaluated regional conduit vessel stiffness in hypertensive ($N=169$) and normotensive ($N=32$) volunteers. Anti-hypertensive medications were stopped >7 days prior to study. Carotid-radial (CR-PWV) pulse wave velocity was used as a measure of peripheral conduit stiffness and carotid-femoral (CF-PWV) pulse wave velocity, characteristic impedance (Z_c) and proximal aortic compliance per unit length (C_f) as measures of central conduit stiffness. All stiffness measures were log transformed to account for nonlinear relations with mean arterial pressure (MAP) and were then adjusted for differences in MAP.

Results: Subjects were 60 ± 8 (45-75) years of age and 62% were male. Central conduit stiffness was markedly increased in hypertensive subjects (Table). In contrast, CR-PWV was normal (Table).

Table. MAP-adjusted hemodynamic parameters (Mean \pm SEM)

	Z_c dyne \cdot sec/cm ⁵	C_f 10 ⁵ cm ⁴ /dyne	CF-PWV m/s	CR-PWV m/s
Hypertension	211 ± 6	0.40 ± 0.02	11.8 ± 0.3	10.5 ± 0.1
Normal	168 ± 14	0.60 ± 0.07	10.0 ± 0.7	11.0 ± 0.4
P	< 0.02	< 0.005	< 0.05	NS

Conclusions: Differential changes in central and peripheral conduits may account for controversy regarding conduit stiffness in hypertension. Elevated central conduit stiffness increases pulse pressure and may contribute to the recently described relationship between pulse pressure and adverse cardiovascular events. Thus, central conduit vessel stiffness may represent an important therapeutic target in hypertension.

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The Cytokine and Soluble Adhesion Molecule Profile in Pediatric Patients With Aortic Coarctation Before and After Successful Surgical Repair

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Background: Increased blood pressure (BP) in hypertensive patients could lead to mechanical impair of vessel wall and endothelium especially and so contribute to initiation of atherosclerotic lesions. Higher concentrations of circulating adhesion molecules and cytokines in patients with essential hypertension were described previously. Their concentration in patients with secondary hypertension due to aortic coarctation (AC) before and long after successful surgical correction were studied.

Patients and methods: 17 pediatric patients with AC were studied. Blood samples were drawn 1d before surgery and 346 \pm 300d during follow-up. Excluded were patients with postoperative persistent hypertension and a need of antihypertensive treatment and patients with severe genetic or connective tissue disease. Serum concentrations of soluble L-, P-, E-selectin, intercellular adhesion molecule-1 (sICAM-1), platelet-cellular adhesion molecule-1 (sPECAM-1) as well as concentrations of cytokines interleukin (IL)-6, IL-8, IL-10 and TNF- α were measured by ELISA.

Results: The surgical correction was successful in all patients, the gradient proximal and distal to AC was 43.09 ± 11.54 mmHg before surgery and not detectable after surgical repair. Both systolic and diastolic BP on arms decreased significantly after surgery ($126.2 \pm 14.6/72.8 \pm 12.8$ mmHg before to $102.5 \pm 9.2/59.4 \pm 7.5$ mmHg after surgery, $p < 0.001$), on legs, systolic but not diastolic BP increased ($90.4 \pm 10.1/59.4 \pm 8.5$ before, $104.7 \pm 11.8/55.8 \pm 6.2$ mmHg after surgery, $p < 0.001$ for systolic values). No differences were found in the concentrations of sE-, P- and L-selectin or sICAM-1, as well as of IL-6 and TNF- α before and after surgery. Serum concentration of sPECAM-1 decreased (59.64 ± 27.1 ng/ml to 42.78 ± 13.31 ng/ml, $p < 0.05$), IL-10 decreased (1.28 ± 1.37 to 0.22 ± 0.41 , $p < 0.05$) and IL-8 increased (2.78 ± 2.9 to 5.88 ± 6.5 , $p < 0.05$) significantly.

Conclusion: Elevated levels of sPECAM-1 in children with AC before surgical correction indicated endothelial activation due to impaired endothelial function. AC is also accompanied with elevated levels of IL-10 and decreased levels of IL-8 indicating their impaired production by leukocytes.

1034-74

Novel Natriuretic Peptide Receptor A Genetic Variant Associated With Higher Blood Pressure Values in Normotensive Subjects

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Background. Experimental studies have suggested that natriuretic peptide receptor A (NPr-A) gene could be a candidate gene in the genesis of essential hypertension. The aim of this study was to evaluate, in normotensive subjects, the association between blood pressure values and a new Insertion/Deletion (Ins/Del) variant, we first identified, in the 3' untranslated region of the NPr-A mRNA.

Methods. In 80 normotensive healthy subjects (mean age 26.3 ± 3.9 years, 40 males) systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse pressure (PP), mean blood pressure (MBP) were obtained. Genomic DNA was isolated according to the standard methods and all subjects were genotyped for the new Ins/Del variant in the 3' untranslated region of the NPr-A mRNA.

Results. Covariance analysis showed significant difference in SBP values independently from age and sex ($F 3.18$; $p < 0.05$). At post-hoc analysis SBP was higher in homozygous than the other two groups (table, * $p < 0.05$ in comparison with heterozygous and normal). No difference was observed in DBP, PP, and MBP values.

Conclusions. This new variant identified in the NPr-A gene is associated with higher blood pressure values suggesting that it may allow the early identification of normotensive subjects prone to develop systemic hypertension.

Genotype	Normal (n=25)	Heterozygous Del (n=40)	Homozygous Del (n=15)
Gender (M/F)	11/14	21/19	8/7
Age (years)	26 ± 3.1	26.7 ± 3.5	25.5 ± 5.7
SBP (mm Hg)	115.8 ± 8.6	116.5 ± 9.4	$122.3 \pm 5.3^*$
DBP (mm Hg)	73.0 ± 7.4	73.6 ± 7.1	74.6 ± 5.9
PP (mm Hg)	43.2 ± 8.5	42.8 ± 7.6	47.7 ± 5.1
MBP (mm Hg)	87.5 ± 6.5	87.8 ± 7.2	90.4 ± 5.2

1034-75

Heritability of Functional Arterial Stiffness: A Twin Study

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Background: The arterial pulse is a result of the interaction between cardiac ejection and the physical properties of the arterial vasculature. Secondary pressure increase measured as augmentation index (AI) has been related to arterial stiffness and wave reflection. This study investigated the heritability of parameters of arterial stiffness in a healthy population of 644 same sex twins (322 pairs, 167 monozygotic, MZ, 155 dizygotic, DZ) age range 19-81 years.

Methods: AI was calculated automatically as the ratio of pressure in late systole to the initial pressure peak in early systole. Central aortic pressure was estimated using transfer function (SphygmoCor, AtCor Medical) from calibrated non-invasive radial pressure waveforms. Pulse wave velocity (an index of arterial stiffness) was measured between the carotid and radial artery (PWVa) and between carotid artery and dorsalis pedis (PWVt). An estimate of heritability (h^2) using the classic twin method was calculated using the intrapair correlation coefficients (r) of MZ and DZ twins, $h^2 = 2 \cdot (r_{MZ} - r_{DZ})$.

Results: All parameters showed significant intrapair correlation (Table). Blood pressure was highly heritable. AI, pulse pressure and PWV also showed significant heritability.

Conclusion: Findings confirm the importance of inheritance on blood pressure and, furthermore, on arterial function. Non-invasive pressure waveform analysis can be used to detect differences in the inherited arterial properties of stiffness and wave reflection.

	rMZ	rDZ	h2
Height	0.97	0.77	0.4
Systolic BP	0.64	0.43	0.42
Radial AI	0.58	0.49	0.18
Central AI	0.66	0.54	0.24
Central pulse pressure	0.6	0.44	0.32
PWVt	0.57	0.47	0.2
PWVa	0.44	0.21	0.46